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THE EFFERENT INNERVATION OF THE VESTIBULAR RECEPTORS

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16. Abstract

The efferent innervation of the vestibular receptors is discussed in the light of current literature and personal experimental findings. Recent studies are reviewed which have demonstrated that nerve fibers subject to acetylcholinesterase activity exist in the acoustic crests and otolithic membranes and that these are efferent fibers. The author's research is based on the fact that the cochlear efferent fibers forming the intraganglionic spiral tract can be distinguished from the afferent fibers by thepositivity of the former to an acetylcholinesterase reaction. Attempts are therefore made to find whether this difference also applies to the vestibular efferent fibers and the afferent fibers.

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THE EFFERENT INNERVATION OF THE VESTIBULAR RECEPTORS

G. Rossi

Recent anatomical, histochemical, experimental and electrophysiological studies have revealed the existence of vestibular fibers following a centrifugal course, with their nucleus of origin in the bulb. The results of these studies should now be complemented by information on the morphology of the vestibular receptors which has been obtained by electron microscopy during the last few years. /230*

The work of Wersäll (1954-1956) has effectively shown the existence of two types of ciliated cells in the acoustic crests of the guinea pig, the cat, and the rat.

The cells of Type I, as classified by Wersäll (1954, 1956), are flask-shaped, and their base is contained in a nerve ending in the form of a calyx which contains a small quantity of granular formations (Wersäll, 1956; Smith, 1956). Observable on the outside of this calyx are other nerve endings which in contrast appear to be provided with a large number of granular formations (Engström, 1958).

The cells of Type II, according to the Wersäll classification (1954-1956), have a cylindrical shape, but their basal part is not contained in a calyx-shaped nerve ending. In the basal part of cells of this type there are nerve endings containing a small quantity of granulations and nerve endings supplied with numerous granular formations of the same type as those observed at the base of the Type I cells (Engström, 1958; Wersäll, 1960) (Fig. 1). The existence of these two types of nerve endings (granular and non-granular) has led Engstrom (1958) to formulate the theory that the nerve endings of the granular type, which have the morphologi-

*Numbers in the margin indicate pagination in the foreign text.

cal characteristics of extrasynaptic endings (Engström, 1958; Wersäll, 1960) are part of the efferent vestibular fibers which Petroff noted for the first time in 1955.

The latter observed that in the cat and the monkey a cross-section of Pair VIII or a median incision in the rhomboid fossa resulted in the disappearance of a system of very fine nerve fibers situated below the acoustic crests and the otolithic membranes. /231

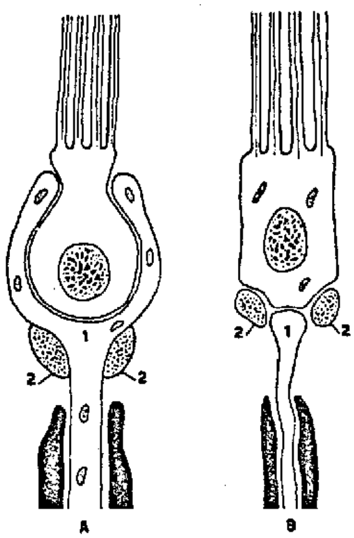

Fig. 1. A. Cell of Type I. 1. Nerve ending in form of a calyx. 2. Nerve endings with a large number of granular formations. B. Cell of Type II. 1. Nerve ending containing a small quantity of granulations. 2. Nerve endings with a large number of granular formations (modified from Wersäll, 1960).

Petroff (1955) states that these efferent fibers follow a crossed path, since a median incision in the rhomboid fossa results in the disappearance of this system of fibers in the two labyrinths.

Rasmussen and Gacek in 1958 and Gacek in 1960 published the results of their work on chinchillas. These investigators studied the phenomena of degeneration of nerve fibers induced by the electrolytic destruction of small areas of the bulb at the level of the vestibular nuclei, or by sagittal incision of the rhomboid fossa at various points.

This research demonstrated the existence of efferent fibers in the vestibular nerve, but it did not confirm the conclusions made by Petroff (1955) in regard to their crossed paths.

Gacek (1960), in fact, believes that there are only direct vestibular fibers, probably originating in the lateral vestibular nucleus.

Results obtained by Nissl chromatolysis after unilateral labyrinthectomy were not sufficient to enable Gacek (1960) to make an exact determination of the origin of the efferent vestibular fibers.

In 1959, Carpenter, Bard and Alling, and in 1960, Carpenter, published the results of a series of experiments performed on cats and monkeys using Nissl chromatolysis after unilateral labyrinthectomy or after sectioning Pairs VII and VIII.

According to these investigators the fastigial nucleus, the medial vestibular nucleus, the superior vestibular nucleus and /232
part of the inferior vestibular nucleus
tibular fibers. The fibers which originate in the fastigial nucleus would primarily be crossed, while those which originate in the above-mentioned vestibular nuclei would

The histochemical research performed by Dohlman, Farkashidy and Salonna (1958) should be mentioned as an adjunct to these anatomical studies. Using the Koelle and Friedenwald technique (1949) for acetylcholinesterase, these investigators have shown the existence of nerve fibers subject to acetylcholinesterase activity below the sensory epithelium of the acoustic crests and the otolithic membranes in the pigeon.

These fibers would exist only in the acoustic crests and the otolithic membranes and would be independent of the vessels. For these reasons, and because of the acetylcholinesterase activity which appears to occur in the fibers, Dohlman, Farkashidy and Salonna (1958) and Dohlman (1960) are of the opinion that these are "efferent cholinergic fibers."

Proof of the efferent nature of these fibers, which are positive to the Koelle and Friedenwald reaction for acetylcholinesterase, has been offered by Ireland and Farkashidy (1961). These investigators demonstrated that sectioning the vestibular branch of Pair VIII in the cat will cause a disappearance of cholinesterase activity in the acoustic crests and the otolithic membranes. /233

In 1962, using the Koelle and Friedenwald reaction in an electron microscopy study, Hilding and Wersäll were able to determine the exact location of the areas positive to this reaction. This interesting study demonstrated that in the acoustic crests, the Koelle and Friedenwald reaction is positive for acetylcholinesterase only in the granular nerve endings located at the base, whether they are cells of Type I or Type II.

The existence of efferent fibers in the vestibular nerve has been confirmed by electrophysiological studies performed by Sala (1962) and Schmidt (1963).

Sala (1962), using square waves to stimulate the rhomboid fossa of the cat in the area where the vestibular nuclei are located, observed the occurrence of a peak potential in the vestibular nerve of the opposite side. This potential was generally positive monophasic and was similar in configuration to the spontaneous potentials. The interval between stimulation and the occurrence of the potential in the vestibular nerve was 22-32 milliseconds.

Schmidt (1963) was able to demonstrate the existence of efferent impulses in *Rana pipiens*, deriving these impulses from the tip of the nerve detached from the ampulla, sacculus, utriculus and lagena. These efferent impulses, which normally do not occur, were produced by stimulating an ampulla or by stimulating certain extralabyrinthine nerve endings which Schmidt (1963) was unable to identify precisely.

Systematic study of the efferent innervation of the vestibular receptors was begun by Rossi in 1960 through a series of histochemical studies, and subsequently continued in a series of embryological studies (1962), anatomical studies performed in collaboration with Cortesina (1962 a, b; 1963; 1964) and experimental studies made in collaboration with Voena, Buongiovanni, and Cortesina (1964).

The point of departure for this work was furnished by an observation made by Rossi in 1960: the cochlear efferent fibers which form the intraganglionic spiral tract can easily be differentiated from the afferent fibers since the former are positive to the Koelle and Friedenwald reaction for acetylcholinesterase.

Rossi therefore proposed to determine whether this difference in regard to the Koelle and Friedenwald reaction for acetylcholinesterase would also occur for the afferent fibers and for the vestibular efferent fibers.

In 1962 Rossi studied the location of acetylcholinesterase during the development of the internal ear in the guinea pig, and using Cajal's reduced silver method he was able to determine that the occurrence of positivity to the Koelle and Friedenwald reaction for acetylcholinesterase in each of the neurosensory structures of the membranous labyrinth is always preceded by the occurrence of positivity to this reaction in a bundle of nerve fibers arriving at each neurosensory structure. /234

The afferent vestibular fibers are negative to the Koelle and Friedenwald reaction for acetylcholinesterase. For the posterior membranous labyrinth it has been possible to show (Rossi, 1962; Rossi and Cortesina, 1962 a, b; 1963) that fibers which are positive to the Koelle and Friedenwald reaction for acetylcholinesterase occur in the terminal branches of the vestibular nerve in the guinea pig only after birth.

In other studies Rossi and Cortesina (1962 a, b; 1963; 1964) have applied the Koelle and Friedenwald reaction for acetylcholinesterase to examination of the bulb in the guinea pig and the rabbit.

Recalling that this reaction was markedly positive only for the efferent vestibular fibers, they intended to use this study to obtain useful information on the origin, course and relationships of the efferent vestibular fibers.

The results of this research were tested by another series of experiments which made use of classical information on the microscopic anatomy of the central nervous system: Nissl coloration, Cajal's reduced silver method, the Nissl chromatolysis method.

Through this series of anatomical, histochemical and experimental studies, Rossi and Cortesina (1962 a, b; 1963; 1964) were able to demonstrate the existence of two bundles of efferent fibers which link the bulb to the posterior membranous labyrinth.

The first of these two bundles originates in a small nucleus which was first noted by Rossi and Cortesina, who designated it the "interposed vestibular nucleus." This nucleus is dorsal to the upper part of the inferior vestibular nucleus, and ventral to the lower part of the lateral vestibular nucleus. This nucleus cannot be identified morphologically, nor with the other principal vestibular nuclei, nor with the other cell groups described above which have close topographical relationships to the principal nuclei.

From this nucleus, which consists of 120 to 150 cells in the guinea pig, originate a bundle of efferent fibers which has been designated by Rossi and Cortesina (1962 a, b; 1963; 1964) as the "ventral direct efferent vestibular tract." /235

The second bundle of efferent fibers which link the bulb to the posterior membranous labyrinth originate in the anterior and inferior part of the lateral vestibular nucleus. This bundle of vestibular efferent fibers, whose course and origin were first shown by Rossi and Cortesina (1962 a, b; 1963), form the "dorsal direct efferent vestibular tract."

According to the data obtained by Rossi and Cortesina (1962 a, b; 1963; 1964), in the efferent innervation of the posterior membranous labyrinth there is also a bundle of fibers which originate in cells of the reticular substance of the pons and the protuberantia, located alongside the median raphe (reticulocochlear and direct vestibular tract) (Fig. 2).

The research performed by Rossi and Cortesina has not shown the existence of crossed vestibular efferent fibers. Rossi and Cortesina (1962 a, b; 1963; 1964) have thus confirmed the results obtained by Ireland and Farkashidy (1961). They have in fact been able to demonstrate that the acetylcholinesterase activity which normally occurs in the acoustic crests and the otolithic membranes is a function of the efferent vestibular fibers. In a final series of experiments, Rossi and Cortesina (1962 a, b; 1963; 1964) observed that a sagittal incision at the lateral angle of the rhomboid fossa, severing the efferent vestibular fibers causes a disappearance of acetylcholinesterase activity in the acoustic crests and the otolithic membranes.

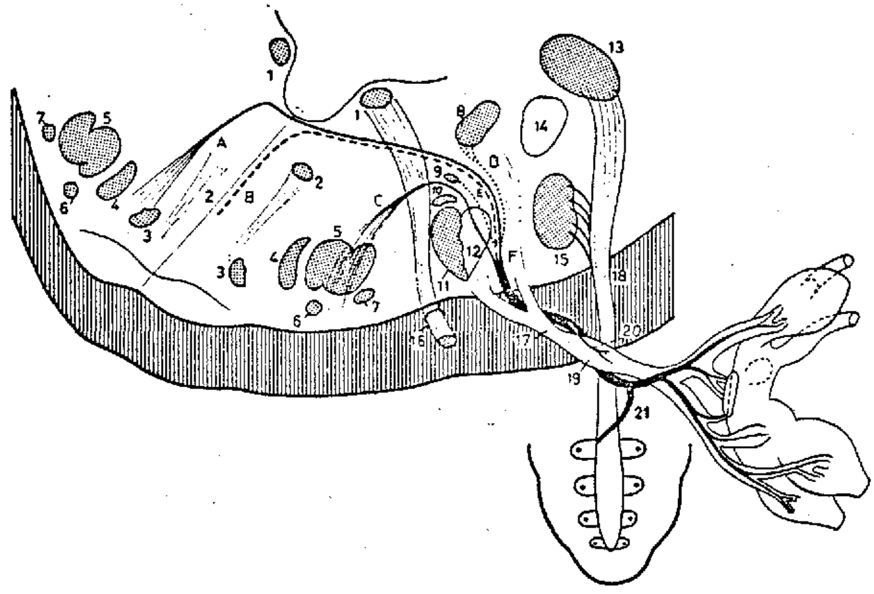

Fig. 2. The system of cochlear and vestibular efferent nerve fibers, after research performed by Rossi and Cortesina. 1. Genu nervi facialis. 2. Nucleus and fibers of Pair VI. 3. Nucleus of trapezoid corpus. 4. Accessory oliva. 5. Lateral superior olivary nucleus. 6. Internal pre-oliva. 7. Lateral pre-oliva. 8. Lateral vestibular nucleus. 9. Interposed vestibular nucleus. 10. Inferior vestibular nucleus. 11. Nucleus of the descending root of the trigeminal nerve. 12. Descending root of the trigeminal nerve. 13. Lateral acoustic tubercle. 14. Pedunculus cerebellaris inferior. 15. Anterior cochlear nucleus. 16. Facial nerve. 17. Vestibular nerve with its superior and inferior roots. 18. Cochlear nerve. 19. Scarpa's ganglion. 20. Efferent fibers ending at Scarpa's ganglion. 21. Oort's anastamosis.

A. Crossed efferent cochlear tract. (——). B. Direct vestibular and reticulo-cochlear tracts. (- - -). C. Direct efferent cochlear tract (——). D. Dorsal direct efferent vestibular tract (...). E. Ventral direct efferent vestibular tract (...). F. Tract consisting of the junction of the cochlear and vestibular efferent nerve fiber bundles (after Rossi and Cortesina, 1964).

All of the research cited above, performed on various species of animals, has shown the existence of a system of efferent nerve fibers with their nucleus of origin in the bulb, linking the bulb to the vestibular receptors.

It can also be inferred from these studies that the most peripheral expansions of the efferent vestibular fibers are located at the base of the Type I or Type II ciliated cells of the acoustic crests, that they are subject to acetylcholinesterase activity, and that this enzyme is present as a function of the integrity of the efferent vestibular fibers.

The presence of acetylcholinesterase in a well-defined point of the group formed by the ciliated cell, the afferent fiber and the efferent fiber presupposes the existence of a mechanism in this area for the transmission of nerve impulses on the basis of the acetylcholine-choline acetylase-acetylcholinesterase system, as a function of the efferent fibers (Fig. 3).

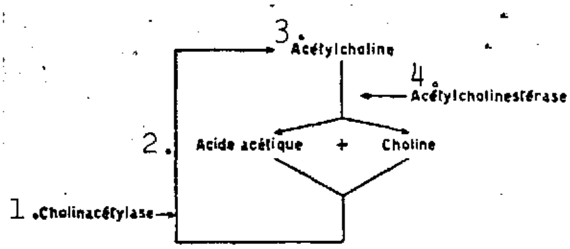

FIG. 3.

Fig. 3.

Key: 1. Choline acetylase.
2. Acetic acid + choline.
3. Acetylcholine.
4. Acetylcholinesterase.

Following this premise, Rossi, Buongiovanni, Cortesina and Voena (1964), in preliminary experiments, studied the effects on vestibular function of the introduction of diisopropyl-fluorophosphate (DFP), a substance derived from anticholinesterase activity, through the carotid artery. These studies were performed on rabbits, whose efferent vestibular innervation is identical to that of the guinea pig, /236
according to the preliminary research performed by Rossi and Cortesina (1964).

The effects of DFP were studied by electronystagmographic recording and were tested using the Koelle and Friedenwald reaction for acetylcholinesterase, induced in the bulb and the acoustic crests.

Through these studies, Rossi, Buongiovanni, Cortesina and Voena (1964) were able to confirm that the introduction DFP through the carotid artery produces a vestibular syndrome in rabbits (the adversive syndrome) which had already been studied by Freedman and Himwich in 1949.

Histochemical tests showed that the positivity of the Koelle and Friedenwald reaction for acetylcholinesterase had appreciably decreased in the half of the bulb on the same side as the common carotid into which the DFP was injected.

In particular, Rossi, Buongiovanni, Cortesina and Voena (1964) were able to observe unilateral disappearance of positivity to the Koelle and Friedenwald reaction for acetylcholinesterase in the efferent vestibular fibers and acoustic crests. Consequently they believe that, even given the possible existence of other mechanisms, the pathogenesis of the vestibular syndrome produced by the introduction of DFP into the carotid artery is at least partly linked to the unilateral reduction in quantity of acetylcholinesterase and the consequent accumulation of acetylcholine which can be observed under these experimental conditions, in the efferent vestibular fibers and the sensory epithelium of the acoustic crests.

The disappearance of positivity to the Koelle and Friedenwald reaction for acetylcholinesterase in the vestibular receptors could be produced either by diffusion of DFP into the endolympha or by destruction of acetylcholinesterase in the efferent vestibular fibers.

Rossi, Voena, Buongiovanni and Cortesina (1964) have successively studied the effects on the vestibular function of rabbits produced by the introduction of anticholinergic compounds (atropine, tetraethylammonium) and substances subject to anticholinesterase activity (diisopropylfluorophosphate) into the acetylcholine endolympha.

These substances were introduced into the endolympha by means of a double fenestration of the lateral semicircular canal, and functional study was performed by electronystagmographic recording.

Keeping in mind the various technical reservations (impossibility of making an exact determination of the amount of each of the substances used which acts on the sensory epithelium) and pharmacological reservations (possibility of direct pharmacodynamic effects or determination of effects in inverse ratio to the concentration of some of the substances used), it seems possible to infer from these experiments that an accumulation of acetylcholine in the efferent synaptic expansions prevents the transmission of afferent impulses by acting on anatomical structures which could not be precisely identified, and which are undoubtedly a part of the system formed by the ciliated cell and /237
the afferent nerve fiber.

The results of these studies also indicate that acetylcholine participates in the mechanism of transmission of nerve impulses from the ciliated cell to the afferent fiber.

The results obtained by Rossi, Voena, Buongiovanni and Cortesina (1964) would thus seem to show that in the sensory epithelium of the acoustic crests, acetylcholine participates in the mechanism which determines and regulates the transmission of afferent impulses.

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